North Methven Street, Perth PH1 5PP, UK

ME RESEARCH UK

breakthrough

News of the ME research YOU are helping to fund

Gibson Parliamentary Inquiry

In June 2006, Dr Vance Spence gave ME Research UK's presentation at the third oral hearing of the Group on Scientific Research into ME (Gibson Parliamentary Inquiry) in the Millbank offices of the House of Commons, London. The Group was established by Dr Ian Gibson, Labour MP for Norwich North, who had been a working scientist himself (latterly Dean of Biology at East Anglia) and head of a research team investigating cancer.

The aim behind the formation of the Gibson Parliamentary Inquiry is to assess the progress of scientific research on ME on behalf of ME patients and researchers alike. The Group scheduled five oral hearings during the summer of 2006, and will publish a report of its findings for public dissemination, to stimulate public debate on the subject and act as a catalyst for increased funding for research into the illness.

Our chairman's presentation was called *ME/CFS scientific research: CMO report and beyond* and contained evidence on the lack of progress since the Chief Medical Officer's report of 2002, specific reasons for the lack of progress (including problems with case definition, the influence of the biopsychosocial model of the illness, the undervaluing of biomedical research findings), and a call for national ring-fencing of funds for biomedical research. A version of his talk can be read on pages 4 and 5.

The photograph shows (L to R) Dr Neil Abbot (our Director of Operations), The Countess of Mar, Dr Vance Spence (our Chairman), Doris Jones (Environmental Issues Forum) and Dr Jonathan Kerr (St George's University of London) outside the House of Lords. ●

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WHAT IS ME/CFS?

Myalgic encephalomyelitis/ encephalopathy (ME) is characterised by a range of neurological symptoms and signs, muscle pain with intense physical or mental exhaustion, relapses, and specific cognitive disabilities.

During the 1990s, the term 'chronic fatigue syndrome' (CFS) came into vogue. Since there was no specific diagnostic test for ME, and since post-exercise 'fatigue' was one of its prominent symptoms, people with ME began to be diagnosed with 'CFS'. At present, efforts are being made to revise the definitions of both ME and CFS, and meanwhile the term ME/ CFS is used.

ME/CFS affects 120,000 to 240,000 people in the UK, and it is classified by the World Health Organisation as a neurological illness (ICD10: G93.3). Most people with ME/CFS are unable to work to full capacity, and 25% are severely disabled, some house or bed-bound. Little support is available to their families and carers. The cause of the illness is unknown, and no cure or universally effective treatment has yet been found.

A report to the Chief Medical Officer of England in 2002 states "ME/CFS is a genuine illness and imposes a substantial burden on the health of the UK population. Improvement of health and social care for people affected by the condition is an urgent challenge."

ME Research UK Research Projects

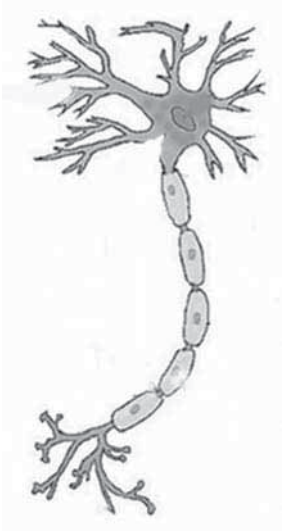
Recently funded work explores key areas in ME/CFS

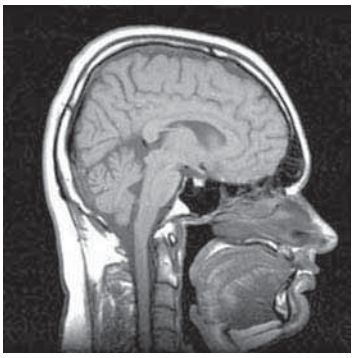
We are currently funding the work of a growing number of scientists whose research covers several different areas of interest. Three of the projects for which we have recently granted funding are briefly described below.

Longitudinal cohort study to determine the prevalence of autonomic dysfunction and relationship with outcome in patients with ME/CFS

Dr Julia Newton, School of Clinical Medical Sciences, University of Newcastle, Newcastle

The researchers will explore the role played by the autonomic nervous system in ME/CFS, using a well-validated battery of autonomic function tests. The intention is to examine 100 ME/CFS patients initially, and — depending on the findings — to monitor their progress over time using further tests.





Non-invasive structural and functional neuroimaging in ME/CFS

Dr Kishore Bhakoo and Professor Basant Puri, MRC Clinical Sciences Centre, Imperial College London, London

Given that research studies have indicated physiological changes in the brains of patients with ME/CFS, this 3-year PhD studentship will use state-of-the-art magnetic resonance imaging techniques to try to identify underlying biological organic mechanisms.

The response of interleukin-6 and its receptors to a standardised exercise challenge

Professor Myra Nimmo, Department of Applied Physiology, University of Strathclyde, Glasgow

This pilot study aims to establish the response of IL-6 and its associated receptors during a submaximal exercise bout in ME/CFS patients and healthy controls over a 24-hour period. The findings may provide data forming the basis of a large programme of research on muscle and nerve function in people with ME/CFS.

ME: A Muscle/Brain Disorder

Epidemics of myalgic encephalomyelitis (ME) were reviewed by Acheson in 1959, and from 1934 to 1959 there were at least 23 well-documented outbreaks of epidemic proportions of a similar illness.

Many of the findings described by Acheson are very much relevant to our understanding of ME today. The disease was initially thought to resemble poliomyelitis until distinguishing features occurred; no patient developed the paralysis and muscle wasting seen in poliomyelitis, a disease of the spinal cord. In essence, Acheson described a systemic infectious illness characterised by marked muscle weakness (not paralysis); muscle pain, tenderness and swelling; and variable involvement of the central nervous system. Henderson and Shelokov, in their review in 1959, also found that the affected muscles were tender either diffusely or in focal discrete areas, which felt "oedematous, doughy or rubbery in consistence". They also mentioned the association of behavioural disturbances with brain cell disorders such as cranial nerve palsies and hemiparesis. Extensor plantar response was an occasional finding in some epidemics, clearly illustrated by Melvin Ramsay in his report of a series of sporadic cases in North West London in 1955/6.

Research funded by ME Research UK has revealed abnormalities in the function of blood vessels and blood cells. However, these have also been described in epidemics. Infectious material was transferred from patients to monkeys during an epidemic in Adelaide, Australia in 1949/50. The only abnormalities discovered at autopsy were minute red spots along the course of the sciatic nerves, found to be localised collections of inflammatory cells which had also infiltrated the area where the nerve roots come out of the spinal cord. Again, during the North of England epidemic in 1955, Andrew Wallis described findings in a patient in her 50s who developed the characteristic febrile illness, leaving her debilitated and emotional. During the next 15 months she continued to run a low grade fever with continued mental deterioration before she died. The post-mortem revealed small haemorrhages around blood vessels in the cerebral cortex extending into the mid-brain, considered to be the cause of her death.

ME is a muscle/brain disorder which occurs as clusters of cases in families, in institutions such as hospitals or schools, and in specific areas, but also sporadically. It is an infectious disease with an incubation period of 5 to 8 days. Acheson used the expression "in a greater or lesser degree" to describe "the symptoms and signs of damage to the brain and spinal cord" in this disease. This expression can also be applied to the febrile illness and muscle involvement. Many patients recover, while others have relapses with reactivation of features of the initial illness and further damage to new areas of the brain or muscles. In extreme cases deterioration may lead to death. After activity, the recovery of muscle power is slower than in any other disease. The association between these findings in muscle and vascular and blood abnormalities needs to be explored. For research purposes, patients with these physical signs should not be coupled with those whose main illness is chronic fatigue on exertion without these signs. ●

This is a summary by Dr Neil Abbot of the review by Dr J Gordon Parish, Patron of ME Research UK, titled "Reflections on The Clinical Syndrome Variously Called Benign Myalgic Encephalomyelitis, Iceland Disease and Epidemic Neuromyasthenia by ED Acheson (American Journal of Medicine 1959)", and available from the Information section of our website.

WHAT IS ME Research UK?

ME Research UK is a medical research charity which commissions and funds scientific (biomedical) investigation into the causes and treatment of ME/CFS. We also have a mission to "Energise ME Research", and our in-house team identifies potentially important biomedical research projects, publishes scientific papers, produces high-quality professional reviews and reports, and organises meetings and conferences.

Recognising that much of the existing research into ME has concentrated on psychological interventions designed to "manage" the illness, ME Research UK believes that biomedical research is urgently required and is what most patients and carers want to see. For this, researchers with fresh, novel ideas have to be recruited and encouraged to undertake research in this field. This is the most difficult task of all, and ME Research UK sees its role at this leading edge: to give help to biomedical scientists for novel research projects that would otherwise not be funded, and to support research groups to the stage where they can apply to major funding agencies for further support based on their initial data.

With your help — and building on our close working relationships with other ME/CFS organisations around the world — ME Research UK can be a force for change, and a source of real hope for the thousands of people with this debilitating illness.

ON THE WEB

www.meresearch.org.uk

ME Research UK's website is a source of news, education and information on ME/CFS research and other issues of interest to biomedical researchers, healthcare professionals, people with the illness and their carers, and the general public.

The **RESEARCH** pages contain summaries and explanations of projects funded by us, reviews of the scientific literature, recently-published ME Research UK articles, and details of our funding procedures.

In the **INFORMATION** section, you can find a collection of literature on ME/CFS and its consequences, a database of abstracts of all ME/CFS research papers from 1956 to 2006, and ME Research UK's own documents discussing and analysing important issues.

The **SUPPORT** section contains information and advice on accessing social care support for people with ME/CFS.

The website also keeps you up-to-date with the latest ME/CFS research news, and with Friends of ME Research UK activities.

ME/CFS Research: CMO

Presentation by Dr Vance Spence to

There are a great many sick people out there — and some have had ME for many years, myself included. Yet they have not lost their spirit, and the fact that this Group has been established is a testament not only to the scale of the problem but also to their feistiness and persistence in the face of great adversity.

The terms of reference for the Group include an assessment of the progress of scientific research, specific reasons for the lack of progress, and an examination of how can we move forward. I propose to address each of these areas in turn.

Progress since the Chief Medical Officer's report of 2002

Progress has been patchy and relatively small-scale. The MEDLINE database lists 783 chronic fatigue syndrome publications during the past 52 months, of which 55 were clinical trials, and only 6 of these were from the UK. Only 57 (vaguely-defined) experimental studies were from the UK, and most of these came from the London Medical Schools in which the biopsychosocial model predominates. Ten discrete studies emanated from 2 privately-funded research groups and another 6 were one-off studies at various locations.

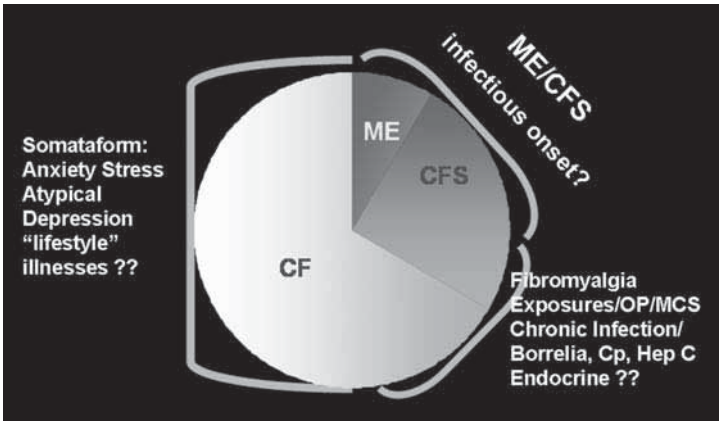
This pattern hardly constitutes an engine room for biomedical investigation of the illness, and compares unfavourably with other illnesses (in the same 52 months there have been 6,231 publications on multiple sclerosis and 48,110 on diabetes). In fact, ME/CFS research is very small-scale, there are comparatively few "biomedical" studies, and while hypotheses abound there is often little data to support them. Any objective observer would conclude that the Chief Medical Officer's report of 2002 has had a minimal effect on the drive to uncover the causes of ME/CFS.

Specific reasons for lack of progress

There many reasons for the lack of progress, but I shall mention briefly 3 central issues.

Case definition issues

ME, CFS and ME/CFS mean different things to different people. This problem colours all debate on ME, yet like the whiteness of a wall it is often not recognised as a colour at all. The pie chart below is an attempt to describe the problem graphically, although the problem may be more or less complex in reality. While the greatest portion of the circle represents the 'set' of patients with chronic fatigue — which might represent 1 to 4% of the population — the set of patients with CFS (i.e., those with 6-months 'fatigue' plus 4 to 8 symptoms) is much smaller (0.2 to 0.4% of the population), while those with ME as described in the older scientific literature might represent a subset of CFS itself, since post-exercise 'fatigue' is a key element in their illness. For researchers the problem is particularly acute since what confidence can they have in the diagnostic discreteness of their patients when the diagnosis "CFS" is so broad?

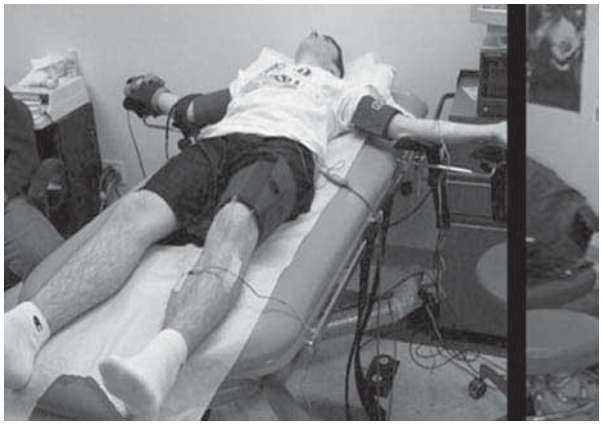


Report and Beyond

the Gibson Parliamentary Inquiry

Influence of the biopsychosocial model of ME/CFS

In most illnesses psychosocial techniques are adjuncts to contemporaneous biomedical research, whereas in ME/CFS the biopsychosocial model seems to have developed a life of its own, hoovering up attention and funding, apparently at the expense of biomedical investigation. As ME Research UK said in a recent letter to the Lancet, *"The central point... is that, for patients with chronic fatigue syndrome (and there are some 20,000 members of support groups in the UK alone), the biopsychosocial model offers relatively little, yet it dominates the canvas in terms of research funding and exposure in professional journals instead of being a small part of the overall clinical and scientific picture."* (Abbot NC, Spence VA. Lancet 2006; 367: 1574)



Biomedical research findings undervalued and unsupported by funding

The third reason for the lack of progress is that biomedical research findings into ME/CFS get ignored and undervalued. Yet they exist, and there is substantial evidence that, despite the apparent heterogeneity of the patient group, biomedical researchers can uncover a range of interesting anomalies. These include anomalies of blood flow to the brain, orthostatic intolerance (see photo above from Prof. JM Stewart, New York Medical College), increased oxidative stress, raised inflammatory markers, and activation of specific genes.

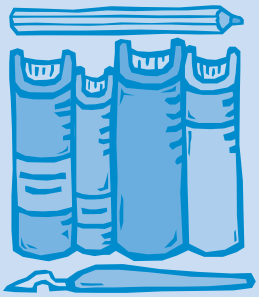
Furthermore, fascinating one-off results covering many of the prominent symptoms of ME/CFS continue to be published by research groups worldwide. These include reduction of brain serotonin transporters in relation to pain (Yamamoto (Burnett et al, 2004) and altered muscle excitability in response to exercise (Jammes et al, 2005). One particular recent one-off finding I'd like to highlight concerns the finding of increased vascular stiffness in ME/CFS patients from my own unit at the University of Dundee, which fits in with our provisional hypothesis that at least some ME/CFS patients might have increased cardiovascular risk.

The key point is that breakthroughs in biomedical research generally follow funding. Yes, many investigations to date have been low-level, and in none of these areas are the findings conclusive as yet. BUT some (or all) of these areas might well lead to a breakthrough in understanding and treating the illness, and without support for biomedical research we will never find out.

Since it is left to the smaller charities to progress the agenda, we do what we can. But much more could and should be done. And the first step is for the larger funding agencies, including the Medical Research Council, to cease being hypnotised by non-curative "incomplete paradigms" and to begin prioritising basic biomedical research by ring-fencing central funds for basic biomedical research. ●

This presentation was given at Westminster in June 2006. The full version is on our website.

MERUK ARTICLES



ME Research UK produces reviews of scientific research into ME/CFS, and publishes general articles on the topic to raise awareness of the issues. Recent examples include:

A Scientific 'Signature' for ME/CFS?
An essay on current developments in genetic research in ME/CFS.

The Muscle in ME: It Isn't All Deconditioning!
A "research update" overview, originally published in the magazine Interaction, in 2005.

New Developments in the Biology of ME/CFS
Our report on the Royal Society of Edinburgh Workshop in 2004.

Severely Overlooked by Science
An overview with the 25% ME Group (with which we have close links) of research on the most severely affected ME/CFS patients.

Advances in the Biomedical Investigation of ME/CFS
Describing some recent developments in biomedical research, as well as some of the problems.

SETTING THE AGENDA

ME Research UK's publications and presentations offering analysis and discussion of public policy issues.

Unhelpful Counsel?
Our response to the CMO's report into the research and treatment of ME/CFS.

Research into ME/CFS in the UK: Can the NRR inform future policy?
Our analysis of ME/CFS research funding sources.

Who Cares?
Our submission on care pathways to the Scottish Executive's Short-Life Action Group on CFS/ME.

Shattered — Life with ME
by Lynn Michell, who collaborated closely with us during the writing of this book. Contains a Foreword and Appendix by ME Research UK.

Cross Party Parliamentary Group on ME
Presentation given in 2005 to the Scottish Parliament by our Chairman Dr Spence.

Database of Research Publications
Contains more than 3,000 research abstracts on ME/CFS, from 1956 to the present.

Most of these and other documents can be found on our website. See the sidebar on page 4.

Recent Research from Around the World

Spectroscopic diagnosis in ME/CFS
A May 2006 report from Osaka University, Japan presents some astonishing results, for the researchers claim to have developed a way to diagnose ME/CFS using visible and near-infrared spectroscopy (Sakudo et al, Biochemical and Biophysical Research Communications 2006). Blood sera from 77 patients and 71 healthy donors were analysed "blind" and the results subjected to principal component analysis (PCA) to examine how sensitive the test was in discriminating between patients and health controls. The PCA model predicted successful discrimination of the masked samples, predicting 54/54 (100%) of healthy donors and 42/45 (93.3%) of ME/CFS patients.

The authors say that their new approach deserves further evaluation as a potential strategy for instrumental diagnosis of CFS. If true, and replicated by other research groups, the findings would be a great advance in the diagnostic armoury for ME/CFS, and — intriguingly — they suggest that unknown factor(s) in blood serum are commonly present in all CFS patients.

Causes of death in ME/CFS patients
Using a memorial list tabulated by the National CFIDS Foundation in the USA, Prof. Jason and colleagues at DePaul University, Chicago (Health Care for Women International 2006) have been examining causes of death among 144 patients for whom sufficient information was available.

As expected, there were approximately three times more women than men (in accord with known gender differences), and the three most prevalent causes of death were heart failure, suicide and cancer (which collectively accounted for 59.6% of all deaths). Interestingly, complications of ME/CFS were reported to be the cause of death in 16/144 (11.1%).

The mean age of those who died from cancer and suicide was 48 and 39 years, respectively, considerably younger than comparable figures (median values 72 and 48 years, respectively) for the general population. Given research by Peckerman and others highlighting potential cardiovascular and cardiac problems among some patients, it is also of note that 20% of the sample was reported to have died of "heart failure".

Genes and ME/CFS
A recent review in an internationally respected journal (Genes and Chronic Fatigue: How Strong Is the Evidence? Science 2006) discussed the significance of the results of a $2 million study of the hypothalamic-pituitary-adrenal axis genes of 58 CFS patients and other control subjects. These results, published in 14 scientific papers in one issue of Pharmacogenomics, found different patterns of expression of about two dozen genes involved in immune function, cell signaling and other roles in patients, leading to claims that solid evidence for a biological basis of CFS has been found.

However, the review cites warnings from other human geneticists that conclusions derived from "gene hunts" carried out on such small samples can be misleading, and that searches of the entire genome (and not just the HPA axis) are needed for the valid identification of disease markers. ●

Colloquium on ME/CFS Biomedical Research

The first Colloquium on ME/CFS Biomedical Research, sponsored jointly by ME Research UK and the Irish ME Trust, took place on Monday 3rd July 2006 at Glasgow Caledonian University (pictured below). The event, hosted by Dr Lorna Paul, consisted of presentations by key scientists with a working interest in the illness, and was followed by a workshop on Physiotherapeutic Aspects of ME/CFS led by Dr Lorna Paul and Dr Jo Nijs from Vrije Universiteit Brussel, Belgium.

The event was targeted particularly at scientific and healthcare professionals with a working interest in ME/CFS, and the aim was to facilitate links between scientists working on the biomedical basis of ME/CFS, and to raise awareness of the need for biomedical investigation.

After a welcome and introduction by Prof. Brian Durward (Dean School of Health and Social Care, Glasgow Caledonian University), there were scientific presentations from, among others, Prof. Jill Belch (Vascular Diseases Research Unit, University of Dundee), Dr Jonathan Kerr (Department of Cellular and Molecular Medicine, St George's University of London) and Dr Julia Newton (School of Clinical Medical Sciences, University of Newcastle).

A professional report consisting of key overview summaries of the presentations will be written and produced by ME Research UK for subsequent distribution to patients, GPs and healthcare professionals. ●

ME Research UK DVD

The short DVD lecture, Energising Biomedical Research in ME/CFS, which we produced earlier in the year has sparked great interest, and to date 4,000 copies have been distrubuted. The film discusses some issues and challenges involved in researching the illness, and gives a brief overview of some of our recent research. Our intention is for this to be the first in a series of films designed to "energise ME research" in its broadest sense.

As Dr Neil Abbot, our Director of Operations, explains, "We have been amazed by the response to the film, as our original intention was simply to make a DVD that could be seen by housebound or bedbound patients. The involvement of the Perth Camcorder Club — a highly professional group of film-making enthusiasts who gave their services free — meant that the final product could be of high quality. The 25% ME Group, with which we have close working links, has sent one to each of its members, and our other Group Friends have been sending copies to their local GP practice managers, so it's been an unforeseen exciting rollercoaster!"

And the moral of this extraordinary response? Surely that there is an enormous pent-up demand out there for good quality information on biomedical research in ME/CFS, and a burning desire among patients and their friends to see fresh, new biomedical research. Copies are still available; contact us for details. ●

A MESSAGE FROM OUR PATRONS

"ME is a substantial medical and social problem, yet relatively little research has been conducted into its causes and consequences.

The Countess of Mar

"A recent report to the Chief Medical Officer said that a programme of research on all aspects of the illness is urgently needed, and that improvement of health and social care is an urgent challenge.

Roger Jefcoate, CBE

"Given the recent sea change in the public perception of ME, and the possibility that ME patients will now be encouraged and supported rather than derided and scorned, we hope that ME Research UK's scientific and policy research will lead the way towards a treatment and cure for people with ME. Please help us to make a real difference to the lives of people with ME."

Standing Order Form

To allow us to press ahead with our mission to Energise ME Research, please consider responding to our Standing Order appeal.

ME Research UK receives no public money and relies entirely on donations from ordinary people. It is vitally important that all our supporters understand that we are one of the very few charities in the world funding biomedical research into ME/CFS, and raising awareness of the issues in a truly professional manner.

Help us to make the breakthrough that patients need and deserve by completing the standing order form on this page, or by donating through the online giving facility via our website.

Please send this form to:

ME Research UK
The Gateway
North Methven Street
Perth PH1 5PP, UK

Tel: 01738 451234
Email: meruk@pkavs.org.uk
www.meresearch.org.uk

For office use only:

Clydesdale Bank
23 South Methven Street, Perth
(82-67-09) for the credit of ME Research UK, a/c no. 50419466

Bank reference number:

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1 **Name** _____

Address _____

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Postcode _____

Telephone _____

E-mail address _____

2 **To the Manager**

Bank/Building Society _____

Branch address _____

_____

Postcode _____

3 **Name of account holder(s)** _____

Account number _____

Branch sort code _____

4 **Please arrange to debit my/our account with the sum of £** _____

On the _____ **day of each month until further notice**

Starting on _____

5 **Pay to: Clydesdale Bank, 23 South Methven Street, Perth PH1 5PQ, UK**

Account: ME Research UK, Account no: 50419466, Branch code: 82-67-09

6 If you are a UK taxpayer, under the Government's Gift Aid scheme ME Research UK can reclaim the tax you have already paid on your gift. This means that your donation can increase by nearly a third at no extra cost to you. It doesn't matter what tax rate you pay as long as you pay an amount of income or capital gains tax equal to the tax we reclaim on your donations in that financial year. Please inform us of changes in your tax status. Please indicate below if you would like ME Research UK to reclaim the tax on your gift.

○ **Please treat this and any future donations I make to ME Research UK, and all payments I have made since 6th April 2000, as Gift Aid donations.**

7 **Signature** _____ **Date** _____

Thank you for your support